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=> fil reg;d l17 ide can tot
FILE 'REGISTRY' ENTERED AT 15:14:04 ON 05 SEP 2004
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STRUCTURE FILE UPDATES:    3 SEP 2004  HIGHEST RN 739335-06-9
DICTIONARY FILE UPDATES:   3 SEP 2004  HIGHEST RN 739335-06-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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Experimental and calculated property data are now available. For more
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to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html


L17  ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   594873-87-7  REGISTRY
CN   19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)-
     (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C21 H28 O2
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PREP (Preparation)

Absolute stereochemistry.
Double bond geometry as shown.
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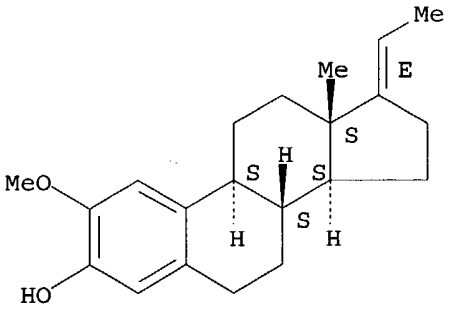


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  139:224972

L17  ANSWER 2 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   438044-29-2  REGISTRY
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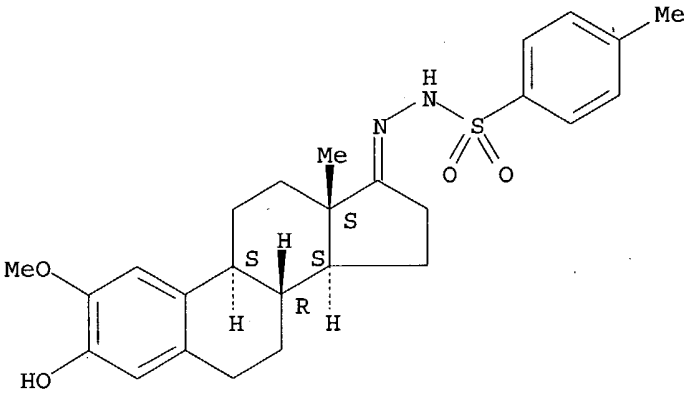
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C26 H32 N2 O4 S**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.



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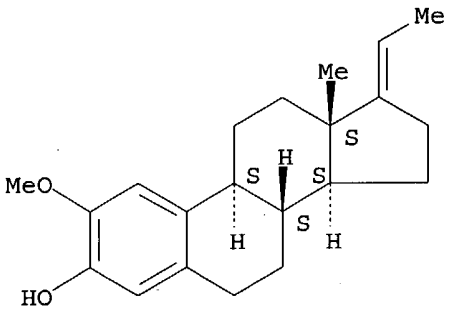
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

L17 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-75-6** REGISTRY
CN **19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C21 H28 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

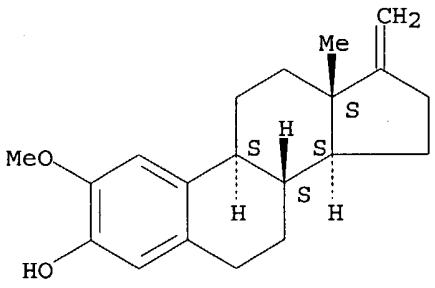
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L17 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-73-4** REGISTRY
CN **Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C20 H26 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:73598

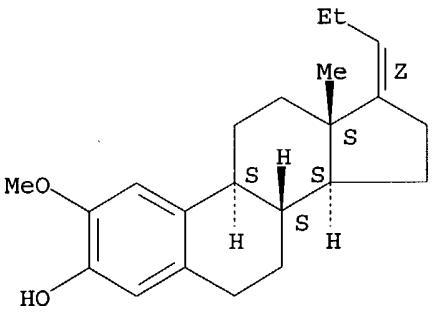
REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L17 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN

RN **431901-72-3** REGISTRY
CN **Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)-**
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C22 H30 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

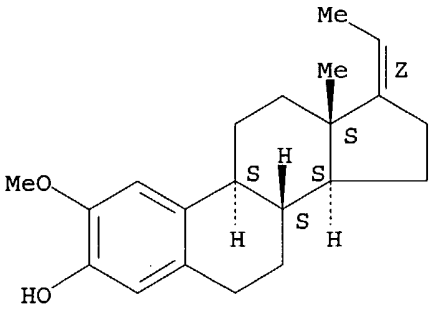
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L17 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 229486-17-3 REGISTRY
CN **19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)-**
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C21 H28 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:73598

REFERENCE 2: 137:370278

REFERENCE 3: 135:358085

REFERENCE 4: 133:350395

REFERENCE 5: 131:88083

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L1 1 S US20020082433/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 15:06:26 ON 05 SEP 2004
L2 68 S E1-E68
L3 63 S L2 AND C5-C6-C6-C6/ES
L4 20 S L3 AND N/ELS
L5 1 S L4 AND S/ELS
E C26H32N2O4S/MF
L6 2 S E3 AND C5-C6-C6-C6/ES
L7 43 S L3 NOT L4
L8 13 S L7 AND 2/O
L9 3 S L8 AND (C20H26O2 OR C22H30O2 OR C21H28O2)
E C20H26O2/MF
L10 432 S E3 AND C5-C6-C6-C6/ES AND 4/NR
L11 146 S L10 AND 4432.3.65/RID
L12 1 S L11 AND 2 METHOXY AND 17 METHYLENE
E C21H28O2/MF
L13 152 S E3 AND 4432.3.65/RID
L14 3 S L13 AND 2 METHOXY
E C22H30O2/MF
L15 110 S E3 AND 4432.3.65/RID
L16 1 S L15 AND 2 METHOXY
L17 6 S L5,L9,L12,L14,L16
SEL RN
L18 0 S E1-E6/CRN

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L19           0 S L17

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L20           8 S L17

     FILE 'USPATFULL, USPAT2' ENTERED AT 15:13:42 ON 05 SEP 2004
L21           4 S L17

     FILE 'REGISTRY' ENTERED AT 15:14:04 ON 05 SEP 2004

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:14:11 ON 05 SEP 2004
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FILE COVERS 1907 - 5 Sep 2004  VOL 141 ISS 11
FILE LAST UPDATED: 3 Sep 2004  (20040903/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L20  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:3558  HCAPLUS
DN   140:73598
ED   Entered STN:  04 Jan 2004
TI   Systems and methods for rapid evaluation and design of molecules for
     predicted biological activity
IN   Hendry, Lawrence B.
PA   USA
SO   U.S. Pat. Appl. Publ., 44 pp.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  A01N001-00
NCL  435001100
CC   9-16 (Biochemical Methods)
     Section cross-reference(s): 1, 3
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 2004002052        A1    20040101    US 2002-279546         20021023
PRAI US 2001-344560P      P     20011023
     US 2001-339954P      P     20011210
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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US 2004002052 ICM A01N001-00
NCL 435001100

AB The computer-based systems and methods are for rapidly evaluating mols. for suspected biol. activity and relative potency, and for designing mols. for desired biol. activity. The systems and methods enable rapid screening of large mol. databases using one or more search engines designed to identify mols. predicted to possess specific biol. activities. Estradiol, 8 other estrogens and the conformation of the DNA site into which they fit were used to construct a search engine which was used to search databases containing a variety of compound structures.

ST system rapid evaluation design mol predicted biol activity; computer system design evaluation biol activity; large mol database search engine biol activity; estrogen search engine screening

IT Named reagents and solutions
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Horeau's acid, identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Antibiotics
(against anthrax, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Bacillus anthracis
(anthrax from, antibiotics against, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Electrostatic potential
(between mol. and binding site, in creating search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Nucleic acids
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(creating search engines for mols. binding specified sites in; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Penis
(erectile activity, evaluation of substances for; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Angiogenesis inhibitors
Antidepressants
Antidiabetic agents
Carcinogens
Hypnotics and Sedatives
Selective estrogen receptor modulators
(evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Androgens
Estrogens
Glucocorticoids
Progestogens
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Bone
Thyroid gland
(evaluation of substances for predicted activity on; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Sexual behavior

(impotence, evaluation of substances for predicted erectile activity and treatment of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Databases
(large mol., systems and methods and search engines for rapid screening of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Information systems
(network; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Information systems
(searching; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Apparatus
Bioinformatics
Computer program
Computers
Conformation
Data processing
Design
Drug design
Excluded volume
Functional groups
Hydrogen bond
Molecular shape
Molecular surface
Molecules
Simulation and Modeling, biological
Simulation and Modeling, physicochemical
Structure-activity relationship
Volume
(systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT DNA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 388075-75-0, PDC 7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDC 7, identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 58-22-0, Testosterone 434-22-0, 19-Nortestosterone 521-11-9, 17α-Methyl-5α-dihydrotestosterone 521-18-6, 5α Dihydrotestosterone 1434-85-1, 5α-Dihydro-19-nortestosterone 3704-07-2, 7α-Methyl-5α-dihydrotestosterone 3704-08-3 3764-87-2, 7α-Methyl-19-nortestosterone 6424-04-0 7642-58-2, 7α-Methyltestosterone 31025-34-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted androgenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 389-08-2, Nalidixic acid 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 79660-72-3, Fleroxacin 85721-33-1, Ciprofloxacin 98079-51-7, Lomefloxacin 100986-85-4, Levofloxacin 110871-86-8, Sparfloxacin 112811-59-3, Gatifloxacin 147059-72-1, Trovafloxacin 151096-09-2, Moxifloxacin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted anthrax antibiotic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 362-07-2, 2-Methoxyestradiol 165619-07-8, 2-Ethoxyestradiol 192062-02-5 **229486-17-3 431901-73-4** 431901-98-3

431902-09-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-48-6, Amitriptyline 50-49-7, Imipramine 303-49-1 5560-72-5, Iprindole 10262-69-8, Maprotiline 24526-64-5, Nomifensin 54910-89-3, Fluoxetine 79617-96-2, Sertraline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted antidepressant activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-28-2, Estradiol, biological studies 57-63-6, 17α-Ethynylestradiol 4567-67-3, 17α-Chloroethynylestradiol 21507-14-2, 11β-Methoxyestradiol 34816-55-2, Moxestrol 95258-49-4 95258-51-8 108887-25-8 130929-98-5 164580-56-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted estrogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-23-7, Cortisol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted glucocorticoid activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 53-43-0, Dehydroepiandrosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted penile erectile and anti-impotence activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 516-54-1, 3α, 5α-Tetrahydroprogesterone 516-55-2 23930-19-0, Alphaxalone 38398-32-2, Ganaxolone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted sedative activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 15178-66-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dbl. stranded, as DNA binding site used in evaluation of substances for predicted anthrax antibiotic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 4251-20-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dbl. stranded, as DNA binding site used in evaluation of substances for predicted estrogenic or androgenic or other activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 3704-09-4, Mibolerone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by androgen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 69-53-4, Ampicillin 28657-80-9, Cinoxacin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by anthrax antibiotic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 54-32-0, Moxisylyte 56-87-1, Lysine, biological studies 74-79-3, Arginine, biological studies 497-76-7, Arbutin 2530-97-4, Xanthinol 7665-99-8, Cyclic GMP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by anti-impotence search engine; systems and methods for

rapid evaluation and design of mols. for predicted biol. activity)

IT 117-39-5, Quercetin 501-36-0, Resveratrol 26581-81-7, EM-12
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by antiangiogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 17692-37-4, Fantridone 34911-55-2, Bupropion 54739-18-3, Fluvoxamine 71620-89-8, Reboxetine 93413-69-5, Venlafaxine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by antidepressant search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 124-87-8, Picrotoxin 5938-11-4, Callicarpone 20071-51-6, Eupatoroxin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by carcinogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 24643-97-8, Indenestrol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by estrogen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 56-53-1, trans-Diethylstilbestrol 446-72-0, Genistein 486-66-8, Daidzein 531-95-3, Equol 26538-44-3, Zearalanol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-35-1, Thalidomide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by sedative and antidepressant and antiangiogenic search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

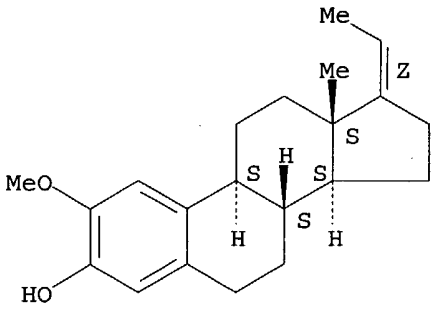
IT 21715-46-8, Etifoxine 61869-08-7, Paroxetine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by sedative and antidepressant search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 57-43-2, Amobarbital 58-61-7, Adenosine, biological studies 73-31-4, Melatonin 77-26-9, Butalbital 1972-08-3, δ9 Tetrahydrocannabinol 20007-85-6, Cyclopenol 57801-81-7, Brotizolam
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identified by sedative search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT **229486-17-3 431901-73-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

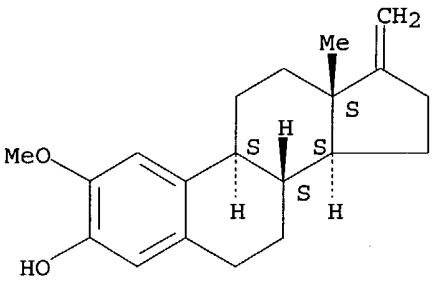
RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719252 HCAPLUS
DN 139:224972
ED Entered STN: 14 Sep 2003
TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents
IN Lavallee, Theresa M.; Pribluda, Victor S.; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi
PA Entremed, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 32
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003073985	A2	20030912	WO 2003-US5898	20030227
WO 2003073985	A3	20031231		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-361267P P 20020301
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003073985	ICM	A61K

AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.
ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha
IT Apoptosis

(2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Cytokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIF-1α (hypoxia-inducible factor 1α); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Blood vessel
(endothelium; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Transcriptional regulation
(of HIF-1α, 2-ME2-inhibited; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Angiogenesis
Angiogenesis inhibitors
Human
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 127464-60-2, Vascular Endothelial Growth Factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions 68-12-2, DMF, reactions 71-36-3, 1-Butanol, reactions 75-09-2, Methylene chloride, reactions 79-37-8, Oxalyl chloride 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 109-99-9, THF, reactions 111-46-6, Diethylene glycol, reactions 121-44-8, Triethylamine, reactions 141-78-6, Ethyl acetate, reactions 302-01-2, Hydrazine, reactions 362-08-3, 2-Methoxyestrone 362-08-3D, 2-Methoxyestrone, olefin analogs 584-08-7, Potassium carbonate 1157-87-5, AH3 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyltriphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4111-54-0, Lithium diisopropyl amide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 7447-41-8, Lithium chloride, reactions 7632-00-0, Sodium nitrite 7693-26-7, Potassium hydride 16853-85-3, Lithium aluminum hydride 17455-13-9, 18-Crown-6 17640-15-2, Methyl cyanoformate 41233-93-6, Potassium-tert-amylate 431901-79-0 431901-81-4 431901-84-7 431901-85-8 431901-89-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

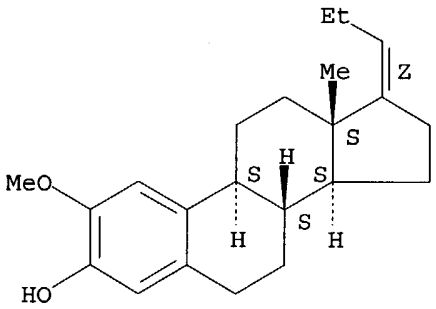
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, alkyl analogs 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P 7291-57-8P 10332-20-4P 26356-54-7DP, alkyl derivs 26356-54-7DP, alkyl derivs. 26356-54-7P 26357-07-3DP, 16α-alkyl derivs. 26357-07-3P 32162-96-2P 34111-53-0P 93949-26-9P 165619-07-8P 229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P **431901-72-3P** 431901-77-8P 431901-78-9P 431901-80-3DP, alkyl derivs. 431901-89-2DP, alkyl analogs 431901-90-5P 431901-91-6P 431901-92-7P 431901-93-8P 431901-98-3P 431901-99-4P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-09-9P 438044-30-5P 464924-32-1P 594873-85-5P 594873-86-6P **594873-87-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT **431901-72-3P 594873-87-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

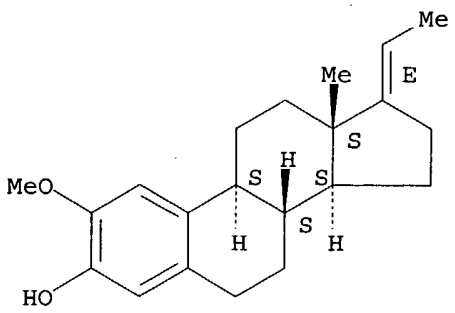
RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 594873-87-7 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L20 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:888569 HCAPLUS

DN 137:370278
ED Entered STN: 22 Nov 2002
TI Preparation of substituted pregna-1,3,5(10)-triene derivatives for pharmaceutical use
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael
PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-56
ICS A61K031-575; C07J041-00; A61P035-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 1

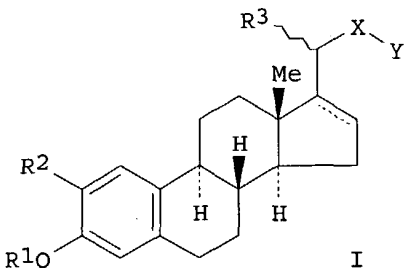
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002092100	A1	20021121	WO 2002-GB2210	20020513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

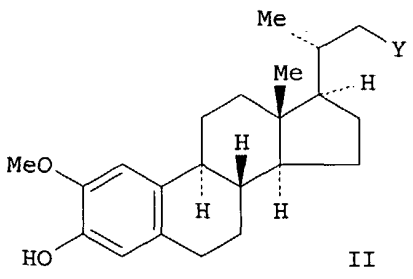
PRAI US 2001-290013P P 20010511
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002092100	ICM	A61K031-56
	ICS	A61K031-575; C07J041-00; A61P035-00

OS MARPAT 137:370278
GI



I



II

AB Pregna-1,3,5(10)-triene derivs., such as I [R1 = H, hydroxy protecting group; R2 = OH, CHO, alkoxy, alkenyl, alkyl, etc.; R3 = α-, β-Me; X = C1-3 alkylene group, bond; Y = C(R4)(R5)NR6R7; R4, R5 = H, alkyl, alkenyl and alkynyl groups, such that the total carbon content of R4 and R5 does not exceed three atoms; R6 = H, aliphatic or araliph. organic group, acyl, etc.; C16-C17 = saturated, unsatd.], were prepared for a variety of therapeutic uses, such as modulating cell activity, including

antiproliferative and antiangiogenic effects. Thus, pregna-1,3,5(10)-triene derivs. II (Y = NH2, NHCOMe) were prepared via a multistep synthetic series starting from 2-methoxy-3-[[tris(1-methylethyl)silyl]oxy]-estra-1,3,5(10)-trien-17-one and ethyltriphenylphosphonium bromide. Pharmaceutical compns. of the prepared compds. were discussed, but specific pharmaceutical activity testing data was not presented.

ST norpregnatriene prepn antiproliferative antiangiogenic agent

IT Mental disorder
(cognitive, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Blood coagulation
Cognition
(disorder, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Anti-inflammatory agents
Anticholesteremic agents
Antitumor agents
Cognition enhancers
Contraceptives
Immunomodulators
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Arthritis
(psoriatic arthritis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Mental disorder
(senile psychosis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Asthma
Autoimmune disease
Bone, disease
Hypercholesterolemia
Hyperplasia
Hypertension
Inflammation
Neoplasm
Rheumatoid arthritis
Skin, disease
Transplant rejection
(treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 4736-60-1, Ethyltriphenylphosphonium iodide 305812-67-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT **229486-17-3P** 305812-87-7P 305812-99-1P 372952-47-1P
372952-49-3P 372952-50-6P 475486-81-8P 475486-82-9P 475486-83-0P
475486-84-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 475486-79-4P 475486-80-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Christopher, M; WO 0068246 A 2000 HCAPLUS

1,3,5(10)-estratriene 3-(2-benzoyl-4-nitro)phenyl ether (VIII), m. 132-44°(MeOH), λ 255, 287 mμ, ε 16,000 and 11,000. Acetylation of VIII with Ac2O in C5H5N gave 16α,17β-diacetoxy-1,3,5(10)-estratriene 3-(2-benzoyl-4-nitro)phenyl ether (IX), m. 74-6° (AcOH), no OH absorption at 3600 cm.-1 IX (1 g.) in 2 cc. AcOH and 2 cc. cold concentrated H2SO4 left 0.5 hr. at room temperature, diluted with 15 ml. AcOH, excess 30% H2O2 added, the solution left 0.5 hr. longer, poured into H2O, the solid collected, and dried gave 750 mg. 2-hydroxy-16α,17β-diacetoxy-1,3,5(10)-estratriene 3-(2-benzoyl-4-nitro)phenyl ether (X), ν 1655 cm.-1 X (0.7 g.) in a min. amount of alc.-Et2O left 24 hrs. with excess CH2N2, and the solvents evaporated gave 2-methoxy-16α,17β-diacetoxy-1,3,5(10)-estratriene 3-(2-benzoyl-4-nitro)phenyl ether (XI), m. 155-8° (MeOH), ν 1672 cm.-1 XI (0.6 g.) refluxed 1 hr. under N with 6% alc.-KOH, acidified, and extracted with CHCl3-Et2O followed by countercurrent distribution in a system of 50% aqueous MeOH and 1:1 cyclohexane-EtOAc gave 180 mg. I, m. 211-14° (dilute Me2CO), [α]26D 83° (alc.), λ 286 and 253 mμ, ε 3500 and 350. IX (5 g.) cyclized and oxidized as above gave the 2-OH product, which, dissolved in alkali, left 15 min., acidified, the product reextd., the crude material taken up in alc., treated with ethereal CH2N2, and the product, m. 160-90°, reacetylated, the total material refluxed 1.5 hrs. in 60 cc. piperidine under N, the solution diluted with 250 cc. C6H6, washed, and the residue chromatographed on Al2O3 gave 0.6 g. 16,17-diacetate of the 3-Me ether of II (XII), m. 178-81 ° (C6H6-ligroine), [α]27D -16.5°.

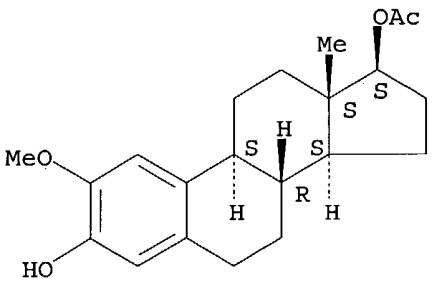
Preceding chromatographic fractions were oils which on hydrolysis with 5% alc.-KOH gave 1 g. 2-methyloxyestriol (XIII). XII (0.5 g.) on hydrolysis in 5% alc.-KOH gave 230 mg. III, m. 268-71° (MeOH-C6H6), [α]25D 64°. III by methylation with CH2N2 gave 3-Me ether of 2-methoxyestriol (XIV), m. 190-2° (Me2CO-ligroine), [α]27D 69°. Similar methylation of XIII gave XIV. 2-Hydroxy-17-acetoxy-1,3,5 (10)-estratriene 3-(2-benzoyl)phenyl ether (XIVa) (8 g.) in Claisen alkali left 15 min. at room temperature, the whole acidified and extracted with CHCl3 gave a crude mixture, which was methylated with CH2N2, the methylated product reacetylated and then refluxed 1 hr. in 100 ml. piperidine, and chromatographed on Al2O3, to give 1 g. 2-methoxyestradiol, 17-acetate (XV). With 50% C6H6-ligroine, 3.1 g. 2-hydroxyestradiol, 3-Me ether 17-acetate (XVI), m. 210-12° (C6H6-ligroine), [α]27D 43.0° was obtained. XVI (1 g.) hydrolyzed in the usual way with 5% alc.-KOH gave 0.85 g. IV, m. 179-81° (Me2CO), [α]28D 74°. Methylation of XVI with Et2O-CH2N2 gave 2-methoxyestradiol 3-Me ether 17-acetate (XVII), m. 179-82°(alc.), [α]27D 53°. A similar methylation of XV gave XVII. Hydrolysis of XVII with MeOH-KOH gave 2-methoxyestradiol 3-Me ether (XVIII), m. 131-3° (MeOH-Et2O), [α]27D 85°. Oxidation of a small amount of XVIII with CrO3 in Me2CO gave VI, needles, m. 173-6°. VI was also obtained by methylation of 2-methoxyestrone (XIX). VI (1 g.) heated 15 min. at 200-20° with 2 g. freshly distilled C5H5N, diluted with H2O, and extracted with CHCl3-alc. gave 700 mg. crude IV, m. 155-8°, [α]28D 90° (alc.), λ 289 mμ, ε 3600. IV was also obtained by an alternate route from XIVa. Piperidine cleavage of XIVa gave 17-acetate of IV, m. 182-5°, [α]26D 59°.

Acid hydrolysis of IV 17-acetate gave IV. XIX (100 mg.) heated with C5H5N.HCl as above and the mixture diluted with H2O gave 63 mg. VII, m. 194-6° (C6H6), [α]27D 172° (alc.). VII was obtained from either I or III on heating 1 hr. at 200° with C5H5N.HCl. An alternative route led via the Schotten-Baumann benzoylation of IV to give the dibenzoate which on oxidation with CrO3 in AcOH gave VII 2,3-dibenzoate, m. 172-4° (alc.). Mild hydrolysis of the above under N gave VII.

C5H5N.HCl-fusion of 200 mg. 3-Me ether of 4-hydroxyestrone gave 138 mg. 4-hydroxyestrone, m. 260-5° (C6H6-MeOH), [α]27D 155° (alc.).

IT Infrared spectra
Ultraviolet and visible, spectra
(of estra-1,3,5(10)-triene-2,3-diol derivs.)
IT Estra-1,3,5(10)-trien-17β-ol, 2,3-dimethoxy-, compound with methanol
Estra-1,3,5(10)-triene-16α,17β-diol, 3-(2-benzoyl-4-nitrophenoxy)-
Estra-1,3,5(10)-triene-16α,17β-diol, 3-(2-benzoyl-4-nitrophenoxy)-, diacetate
Estra-1,3,5(10)-triene-16α,17β-diol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-, diacetate
Estra-1,3,5(10)-triene-2,16α,17β-triol, 3-(2-benzoyl-4-nitrophenoxy)-, 16,17-diacetate
Methanol, compound with 2,3-dimethoxyestra-1,3,5(10)-trien-17β-ol
IT Estra-1,3,5(10)-triene-2,3-diol
(derivs.)
IT 362-05-0, Estra-1,3,5(10)-triene-2,3,17β-triol 362-06-1, Estra-1,3,5(10)-trien-17-one, 2,3-dihydroxy- 1236-72-2, Estriol, 2-methoxy- 3131-23-5, Estra-1,3,5(10)-trien-17-one, 3,4-dihydroxy- 5976-64-7, Estra-1,3,5(10)-trien-17-one, 2,3-dimethoxy- 5976-65-8, Estra-1,3,5(10)-triene-2,17β-diol, 3-methoxy- 5976-67-0, Estra-1,3,5(10)-trien-17β-ol, 2,3-dimethoxy- 5976-70-5, Estra-1,3,5(10)-trien-17β-ol, 2,3-dimethoxy-, acetate 21696-98-0, Estra-1,3,5(10)-triene-16α,17β-diol, 2,3-dimethoxy- 23463-05-0, Estra-1,3,5(10)-triene-2,3,17β-triol, 17-acetate 28818-82-8, Estra-1,3,5(10)-triene-2,16α,17β-triol, 3-methoxy- **52717-98-3**, Estradiol, 2-methoxy-, 17-acetate 52717-99-4, Estra-1,3,5(10)-triene-2,17β-diol, 3-methoxy-, 17-acetate 59495-33-9, Estra-1,3,5(10)-triene-2,16α,17β-triol, 3-methoxy-, 16,17-diacetate 116282-36-1, Estra-1,3,5(10)-trien-17-one, 2,3-dihydroxy-, dibenzoate 117921-01-4, Benzophenone, 2-(16α,17β-dihydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro- 121212-59-7, Benzophenone, 2-(16α,17β-dihydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, diacetate 122426-55-5, Benzophenone, 2-(16α,17β-dihydroxy-2-methoxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, diacetate
(preparation of)
IT **52717-98-3**, Estradiol, 2-methoxy-, 17-acetate
(preparation of)
RN 52717-98-3 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

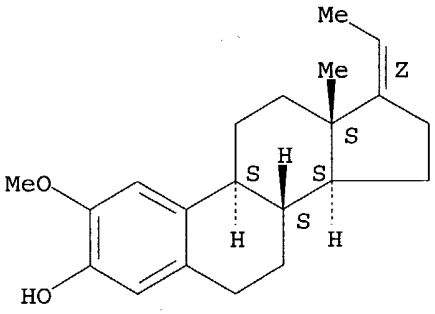


L30 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1958:77293 HCAPLUS
DN 52:77293
OREF 52:**13765i,13766a-h**
ED Entered STN: 22 Apr 2001
TI Synthesis of 2-methoxyestrogens

AU Fishman, Jack
CS Sloan-Kettering Inst. for Cancer Research, New York, NY
SO Journal of the American Chemical Society (1958), 80, 1213-16
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA Unavailable
CC 10 (Organic Chemistry)
OS CASREACT 52:77293
AB Estrone (I) (1.71 g.) added to 0.210 g. KOH in 50 cc. absolute EtOH, warmed, treated with 0.853 g. 2,5-Cl(O2N)C6H3Bz (II), refluxed 24 hrs., concentrated to half the original volume, cooled, poured into N NaOH, extracted with CHCl3, and the extract evaporated yielded 1.365 g. 3-(2-benzoyl-4-nitrophenyl) ether (III) of I, m. 240-3° (MeOH), [α]26D 88°; the aqueous alkaline solution acidified gave 0.7 g. unchanged I. III (100 mg.) in 0.5 cc. cold. concentrated H2SO4 treated after 0.5 hr. with 4 cc. glacial AcOH then with 0.5 cc. 30% H2O2, allowed to stand 0.5 hr., poured into iced H2O, filtered, the solid washed with H2O, treated with excess CH2N2 in Et2O, the resulting needles, m. 144-7°, refluxed 1 hr. with piperidine, diluted with C6H6, washed with dilute H2SO4, the C6H6 layer extracted with dilute aqueous NaOH, and the aqueous extract acidified and extracted with CHCl3 gave a few crystals of the 13,17-secolactone, m. 204-7°. 17β-Estradiol (IV) (5 g.) and 0.586 g. KOH in 100 cc. EtOH refluxed 48 hrs. with 2.4 g. II, concentrated to half the original volume, poured into 200 cc. N NaOH, extracted with CHCl3, the extract dried, evaporated, and the residual viscous oil dissolved in 50 cc. 1:1 petr. ether-C6H6 and chromatographed on 150 g. Al2O3 gave 90 mg. II, m. 114-16°, and 4.12 g. 3,17β-dihydroxy-1,3,5-(10)-estratriene 3-(2-benzoyl-4-nitrophenyl) ether (V), m. 97-105°, [α]26D 40°. V was oxidized in excellent yield to III. Further elution of the column with Et2O gave some unreacted IV. V with Ac2O and pyridine gave the acetate (VI) of V, viscous oil. VI (7.5 g.) in 4 cc. glacial AcOH treated slowly with cooling and shaking with 10 cc. cold concentrated H2SO4, kept 0.5 hr. at room temperature, diluted with 40 cc. glacial AcOH, treated dropwise with 10 cc. 1:1 AcOH-30% H2O2, kept 0.5 hr. at room temperature, poured into iced H2O, and filtered gave 4.6 g. 2-OH derivative (VII) of VI, m. 170-2° (MeOH), [α]28.8D 21.0°; 2nd crop, 1.6 g. VII (2.2 g.) in 50 cc. EtOH kept 24 hrs. at 5° with excess CH2N2 in Et2O and evaporated gave 2 g. 2-MeO analog (VIII) of VII, m. 169-71°, [α]26D 36°. VIII (432 mg.) refluxed 1 hr. in 20 cc. pyridine, diluted with 100 cc. C6H6, washed with dilute H2SO4 and N NaOH, evaporated, and the oily residue (446 mg.) chromatographed on 16 g. Al2O3 yielded 180 mg. 2-methoxy-3-hydroxy-17β-acetoxy-1,3,5(10)-estratriene (IX), plates changing to needles, m. 194-6° (C6H6-petr. ether), [α]26D 125°. IX hydrolyzed under N with 5% alc. KOH gave 2-methoxy-17β-estradiol (X), m. 184-6° (C6H6). VIII (1.43 g.) in 50 cc. 6% alc. KOH refluxed 2 hrs. under N, diluted with H2O, and extracted with C6H6 gave 700 mg. X, blades, m. 188-90° (Me2CO), [α]21D 100°; diacetate of X, needles, m. 165-6° (MeOH), [α]26.5D 53°. X partially dissolved in N NaOH and shaken with excess BzCl gave 3-monobenzoate (XI) of X, m. 195-8° (MeOH), [α]28D 72°. VIII (203 mg.) in 40 cc. EtOH containing 8 cc. concentrated H2SO4 refluxed 24 hrs., diluted with H2O, extracted with Et2O, and the extract worked up gave 180 mg. 2-MeO derivative (XII) of V, m. 125-6° (MeOH), [α]28D 61°, also obtained in considerably lower yield by alkaline hydrolysis of VIII at room temperature XII (290 mg.) in 40 cc. Me2CO treated dropwise with 8N CrO3-H2SO4 until an orange-brown color persisted, kept 15 min. at room temperature, poured into H2O, and extracted with CHCl3 yielded 231 mg. 2-MeO derivative (XIII) of I, needles, m. 204-5° (MeOH),

(2) Christopher, M; WO 0185755 A 2001 HCAPLUS
(3) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS
(4) Jacques, P; US 3291690 A 1966
IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)
RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L20 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:488275 HCAPLUS
DN 137:47357
ED Entered STN: 28 Jun 2002
TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents
IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony M.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07J041-00
ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00
NCL 552544000
CC 32-3 (Steroids)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002082433	A1	20020627	US 2001-939208	20010824
PRAI	US 2000-641327	A2	20000818		
	US 2000-253385P	P	20001127		
	US 2000-255302P	P	20001213		
	US 2001-278250P	P	20010323		
	US 2001-933894	A2	20010821		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002082433	ICM	C07J041-00
	ICS	C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00

NCL 552544000
OS MARPAT 137:47357
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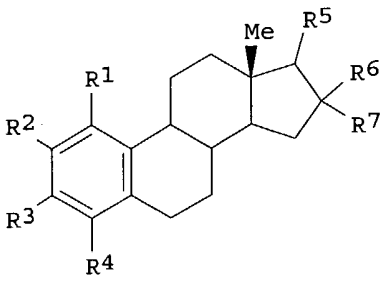

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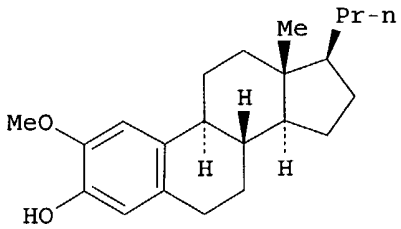


II

AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31 μM.

ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn

IT Structure-activity relationship
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Antitumor agents
Human
Mammary gland, neoplasm
Neoplasm
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P **431901-72-3P** **431901-73-4P** **431901-75-6P** 431901-77-8P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P 165881-61-8P 229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P 431901-74-5P 431901-78-9P 431901-87-0P 431901-90-5P 431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P **438044-29-2P** 438044-30-5P 438044-35-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

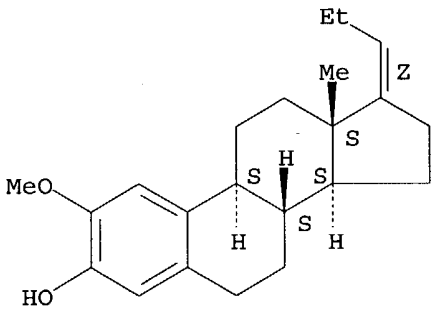
IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions 1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P 431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P 438044-31-6P 438044-32-7P 438044-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **431901-72-3P 431901-73-4P 431901-75-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

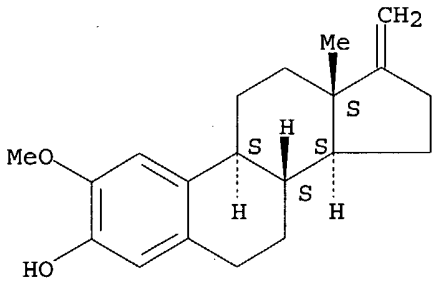
RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-75-6 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

WO 2002042319 A3 20030313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2001088386 A5 20020603 AU 2001-88386 20010824
EP 1343803 A2 20030917 EP 2001-968112 20010824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-253385P P 20001127
US 2000-255302P P 20001213
US 2001-278250P P 20010323
US 2001-933894 A 20010821
WO 2001-US26490 W 20010824

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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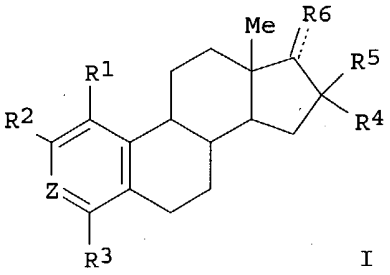
OS MARPAT 137:6309

GI



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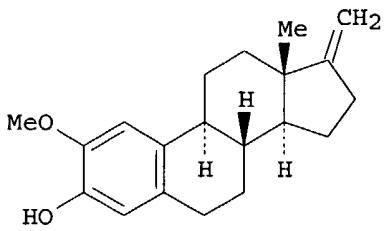


II

AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH2OH, NH2, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC50 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation
(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents
(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Human

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol **431901-72-3P**
431901-73-4P 431901-75-6P 431901-77-8P 431901-83-6P
431901-89-2P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P
7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P
165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P 431901-68-7P
431901-69-8P 431901-70-1P 431901-71-2P 431901-74-5P 431901-76-7P
431901-78-9P 431901-82-5P 431901-84-7P 431901-86-9P 431901-87-0P
431901-88-1P 431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P
431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P
431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P
431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

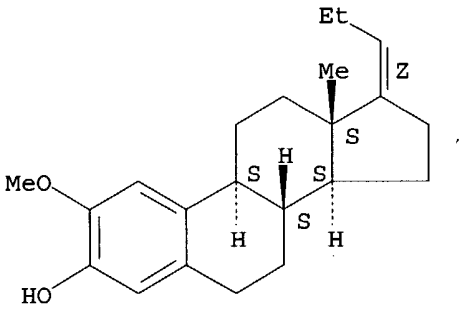
IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2, 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P
431901-81-4P 431901-85-8P 431901-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **431901-72-3P 431901-73-4P 431901-75-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

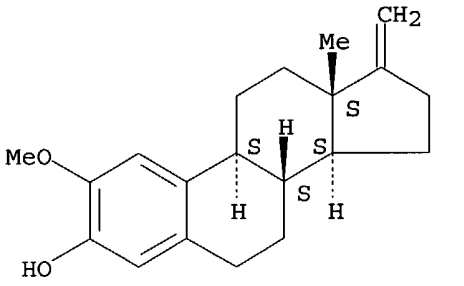
RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



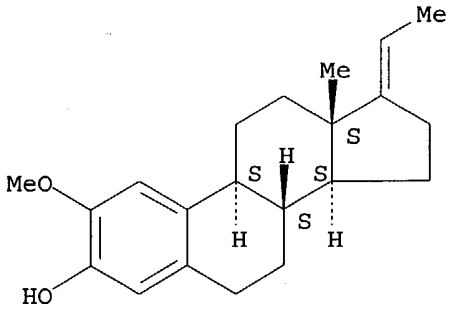
RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-75-6 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L20 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:833342 HCAPLUS
DN 135:358085
ED Entered STN: 16 Nov 2001
TI Preparation of 2-substituted pregna-1,3,5(10)-triene and chola-1,3,5(10)-triene derivatives with antiproliferative and antiangiogenic activity
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael
PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001085755	A1	20011115	WO 2001-GB2103	20010511
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1287017	A1	20030305	EP 2001-928120	20010511
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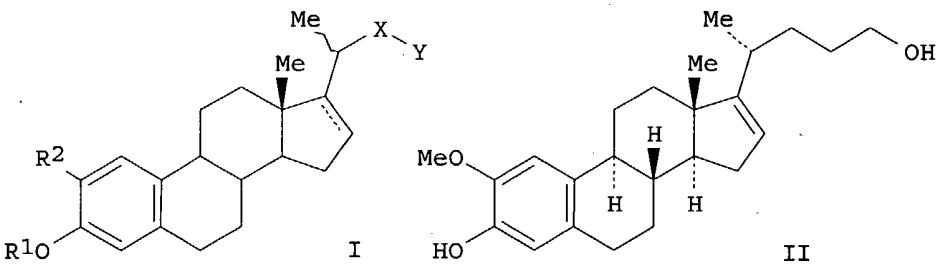
JP 2003532737	T2	20031105	JP 2001-582354	20010511
NZ 523042	A	20040528	NZ 2001-523042	20010511
NO 2002005392	A	20030109	NO 2002-5392	20021111
US 2003158167	A1	20030821	US 2003-275257	20030313
PRAI US 2000-203462P	P	20000511		
WO 2001-GB2103	W	20010511		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001085755	ICM	C07J041-00
	ICS	A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00

OS MARPAT 135:358085

GI



AB Compds. of formula I [R1 = H, protecting group; R2 = OH, alkoxy, CHO, alkenyl, etc.; X = alkylene, bond; Y = CHO, (substituted) CH2OH, etc.] are prepared which exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects. Thus, 2-methoxy-3-triisopropylsilyloxy-19-norpregn-1,3,5(10),17(20)Z-tetraene (preparation given) is reacted with Me acrylate, reduced with LiAlH4, and desilylated with TBAF to give II.

ST pregnatriene deriv prepn antiproliferative antiangiogenic; cholatriene deriv prepn antiproliferative antiangiogenic; antiproliferative

pregnatriene cholatriene deriv; antiangiogenic pregnatriene cholatriene deriv

IT Angiogenesis inhibitors
Antitumor agents
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT Proliferation inhibition
(proliferation inhibitors; preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-25-5P 372952-27-7P 372952-29-9P 372952-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-23-3P 372952-24-4P 372952-28-8P 372952-31-3P 372952-32-4P
372952-33-5P 372952-34-6P 372952-35-7P 372952-36-8P 372952-37-9P
372952-38-0P 372952-39-1P 372952-40-4P 372952-41-5P 372952-42-6P
372952-43-7P 372952-44-8P 372952-45-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 96-33-3, Methyl acrylate 305812-67-3 372952-58-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT **229486-17-3P** 305812-87-7P 305812-89-9P 305812-91-3P
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372952-55-1P 372952-56-2P 372952-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

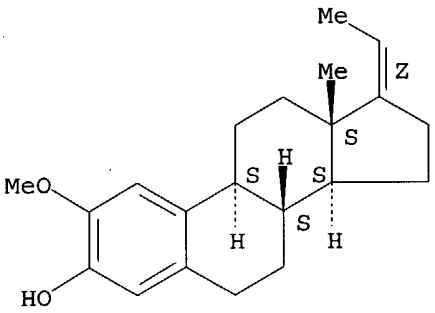
(1) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS
(2) Marsden, J; WO 0068246 A 2000 HCAPLUS
(3) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A HCAPLUS
(4) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A HCAPLUS
(5) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A HCAPLUS
(6) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A HCAPLUS
(7) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A HCAPLUS
(8) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A 1979 HCAPLUS
(9) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A 1979 HCAPLUS
(10) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A 1979 HCAPLUS
(11) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A 1979 HCAPLUS
(12) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A 1979 HCAPLUS
(13) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(14) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(15) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA

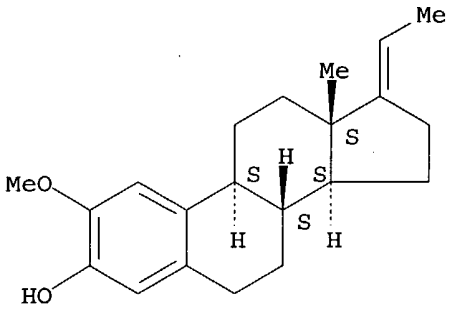
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



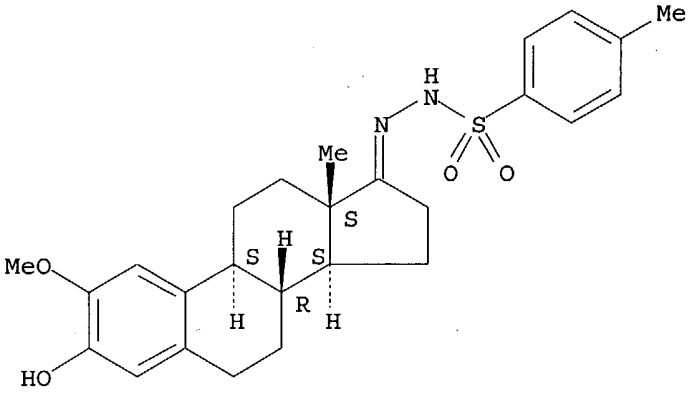
L20 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:814500 HCAPLUS
DN 133:350395
ED Entered STN: 21 Nov 2000
TI Synthesis of cholestane compounds with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Ramgopal, Malathi; Kugabalusooriar, Sanga
PA Marsden, John, Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J009-00
ICS C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10; A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06; A61P025-28; A61P015-18; A61P007-02; A61P003-06
CC 32-7 (Steroids)
Section cross-reference(s): 1, 2
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000068246	A1	20001116	WO 2000-GB1813	20000511
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1179005	A1	20020213	EP 2000-927569	20000511
EP 1179005	B1	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 254629	E	20031215	AT 2000-927569	20000511
PT 1179005	T	20040430	PT 2000-927569	20000511
NZ 515482	A	20040528	NZ 2000-515482	20000511
ES 2207509	T3	20040601	ES 2000-927569	20000511
ZA 2001009272	A	20021128	ZA 2001-9272	20011109



IT **438044-29-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 438044-29-2 HCAPLUS
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L20 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:408687 HCAPLUS
DN 137:6309
ED Entered STN: 31 May 2002
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents
IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony
PA Entremed, Inc., USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J001-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824

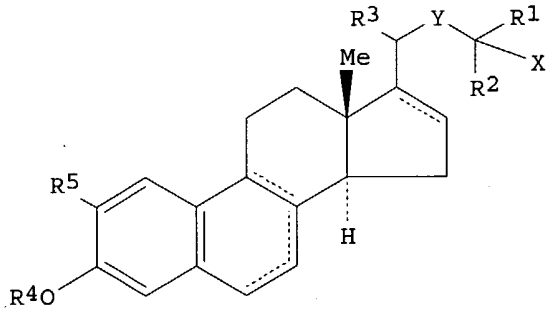
	NO 2001005520	A	20020109	NO 2001-5520	20011112
PRAI	GB 1999-10934	A	19990511		
	WO 2000-GB1813	W	20000511		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000068246	ICM	C07J009-00
	ICS	C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10; A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06; A61P025-28; A61P015-18; A61P007-02; A61P003-06

OS MARPAT 133:350395

GI



I

AB Synthesis of cholestane compds. (I) [R1 and R2, which may be the same or different, = alkyl, alkenyl, alkynyl; R3 = Me having α- or β-configuration; R4 = H or an etherifying or esterifying group; R5 = H, OH, alkoxy; X = OR4, wherein R4 is as defined above, or NR6R7 wherein R6 = H, aliphatic or araliph. organic group, acyl group comprising aliphatic, araliph. or aryl organic group linked to the nitrogen atom by way of a carbonyl group; R7 = H, alkyl; Y = (un)substituted alkylene, alkenylene, alkynylene; dotted lines signify that double bonds may be present at the 16(17)-position and/or either at the 6(7)- and 8(9)-positions or at the 7(8)-position] is disclosed for modulation of cell growth and differentiation, while having low calcemic activity. Thus, I [R1,R2 = Me; R3 = α-Me; R4,R5 = H; X = NHAc; Y = (CH2)4; Δ16 double bond] is prepared by reaction of 3-triisopropylsilyloxy-19-norchol-1,3,5(10),16-tetraene-24-bromide with acetoniltrile followed by reduction of nitrile to amine, methylation of amine with Me lithium, acetylation of the amino with acetic anhydride and desilylation with TBAF.

ST cholestane analog prepn cell growth modulation differentiation; low calcemic activity cholestane analog

IT Steroids, preparation
Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Transplant and Transplantation
(host-vs.-graft reaction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Arthritis
(psoriatic arthritis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Hyperparathyroidism

(secondary; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Mental disorder
(senile psychosis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Heart, disease
(spondylitic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Aromatic hydrocarbons, preparation
Aromatic hydrocarbons, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(steroids; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Anti-inflammatory agents
Antitumor agents
Asthma
Autoimmune disease
Blood coagulation
Bone, disease
Burn
Fertility
Hyperplasia
Hypertension
Intestine, disease
Muscle, disease
Rheumatoid arthritis
Skin, disease
Transplant rejection
Wound healing
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood reduction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(suppression; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-17-3P 305812-18-4P 305812-52-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-19-5P 305812-20-8P 305812-21-9P 305812-22-0P 305812-23-1P
305812-24-2P 305812-25-3P 305812-26-4P 305812-27-5P 305812-28-6P
305812-29-7P 305812-30-0P 305812-31-1P 305812-32-2P 305812-33-3P
305812-34-4P 305812-35-5P 305812-36-6P 305812-37-7P 305812-38-8P
305812-39-9P 305812-40-2P 305812-41-3P 305812-42-4P 305812-43-5P
305812-44-6P 305812-45-7P 305812-46-8P 305812-47-9P 305812-48-0P
305812-49-1P 305812-50-4P 305812-51-5P 305812-53-7P 305812-54-8P
305812-55-9P 305812-56-0P 305812-57-1P 305812-58-2P 305812-59-3P
305812-60-6P 305812-61-7P 305812-62-8P 305812-63-9P 305812-64-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 74-88-4, Methyl iodide, reactions 75-03-6, Ethyl iodide 75-05-8,

Acetonitrile, reactions 78-77-3, Isobutyl bromide 96-33-3 98-88-4, Benzoyl chloride 103-80-0, Phenylacetyl chloride 106-96-7, Propargyl bromide 474-87-3 517-09-9 867-13-0 922-67-8, Methyl propiolate 1439-36-7, 1-Triphenylphosphoranylidene-2-propanone 3234-64-8, 1,1-Diethylpropargylamine 4736-60-1, Ethyl triphenylphosphonium iodide 7103-48-2, Estrone-3-tetrahydropyranyl ether 17963-41-6 305812-65-1 305812-66-2 305812-67-3 305812-69-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT **229486-17-3P** 305812-70-8P 305812-71-9P 305812-72-0P
305812-73-1P 305812-75-3P 305812-76-4P 305812-77-5P 305812-79-7P
305812-81-1P 305812-83-3P 305812-85-5P 305812-87-7P 305812-89-9P
305812-91-3P 305812-93-5P 305812-95-7P 305812-97-9P 305812-99-1P
305813-01-8P 305813-03-0P 305813-05-2P 305813-07-4P 305813-09-6P
305813-10-9P 305813-12-1P 305813-14-3P 305813-15-4P 305813-16-5P
305813-17-6P 305813-19-8P 305813-20-1P 305813-21-2P 305813-22-3P
305813-23-4P 305813-25-6P 305813-26-7P 305813-27-8P 305813-28-9P
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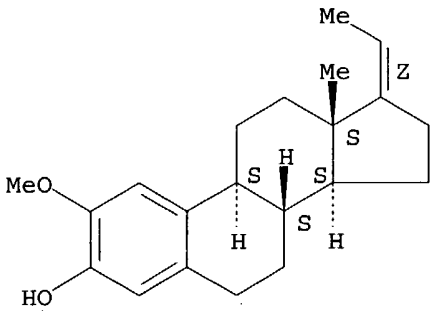
305813-54-1P 305813-55-2P 305813-56-3P 305813-57-4P 305813-58-5P
305813-59-6P 305813-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Escaleira; 1993, 7, HCAPLUS
(2) Escaleira; J STEROID BIOCHEM MOL BIOL 1993, V45(4), P257 HCAPLUS
(3) Laing, S; US 3717627 A 1973
(4) Lajeunesse; 1994, 23, HCAPLUS
(5) Lajeunesse; BONE MINER 1994, V24(1), P1 HCAPLUS
(6) Liel; 1992, 25, HCAPLUS
(7) Liel; ENDOCRINOLOGY (BALTIMORE) 1992, V130(5), P2597 HCAPLUS
(8) Mountford; 1999, 8, HCAPLUS
(9) Mountford; EXP HEMATOL (N Y) 1999, V27(3), P451 HCAPLUS
(10) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



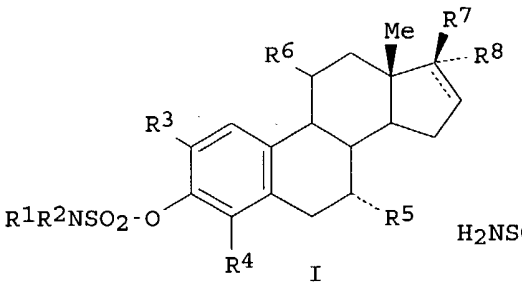
L20 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:460438 HCAPLUS
DN 131:88083
ED Entered STN: 28 Jul 1999
TI Preparation of estrone sulfamate inhibitors of estrone sulfatase
IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko
PA SRI International, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS A61K031-565; A61K031-57; A61K031-575
CC 32-3 (Steroids)
Section cross-reference(s): 2, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933858	A2	19990708	WO 1998-US27333	19981221
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046186	A	20000404	US 1997-997416	19971224
	CA 2318349	AA	19990708	CA 1998-2318349	19981221
	AU 9919416	A1	19990719	AU 1999-19416	19981221
	AU 751732	B2	20020829		
	EP 1042354	A2	20001011	EP 1998-964243	19981221
	EP 1042354	B1	20040303		
	R: DE, FR, GB, IT, NL				
	JP 2001527089	T2	20011225	JP 2000-526534	19981221
	EP 1405860	A1	20040407	EP 2003-28361	19981221
	R: DE, FR, GB, IT, NL				
PRAI	US 1997-997416	A	19971224		
	EP 1998-964243	A3	19981221		
	WO 1998-US27333	W	19981221		

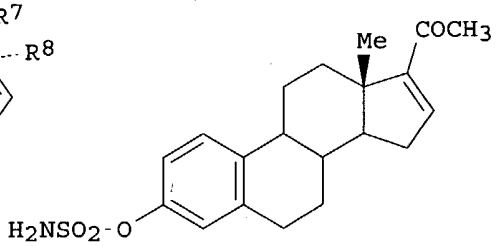
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9933858	ICM	C07J041-00
	ICS	A61K031-565; A61K031-57; A61K031-575
WO 9933858	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
US 6046186	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70
EP 1405860	ECLA	C07J041/00B; C07J041/00C40; C07J041/00C70

OS MARPAT 131:88083
GI



I



II

AB Novel compds.of formula I [R1, R2 = H, alkyl, etc.; R3 = H, CN, NO2, COOH, alkoxycarbonyl, etc.; R4 = H, NO2, (substituted) amino; R5, R6 = H, alkyl; R7, R8 = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R7,R8 = oxo, alkylidene, etc.] are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynylestradiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC50 = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.

ST estrone sulfamate prepn estrone sulfatase inhibitor

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT Antitumor agents
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 185910-34-3P 185910-42-3P 208924-86-1P 208924-87-2P 229485-78-3P
229485-79-4P 229485-80-7P 229485-81-8P 229485-82-9P 229485-83-0P
229485-84-1P 229485-85-2P 229485-86-3P 229485-87-4P 229485-88-5P
229485-89-6P 229485-90-9P 229485-91-0P 229485-92-1P 229485-93-2P
229485-94-3P 229485-95-4P 229485-96-5P 229485-97-6P 229485-98-7P
229485-99-8P 229486-00-4P 229486-01-5P 229486-02-6P 229486-03-7P
229486-04-8P 229486-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6, Ethynylestradiol 108-01-0, N,N-Dimethylethanolamine 109-77-3, Malononitrile 362-08-3 867-13-0, Triethylphosphonoacetate 1779-51-7, Butyltriphenylphosphonium bromide 4584-46-7 5407-04-5 6228-47-3, Propyltriphenylphosphonium bromide 7678-95-7 67530-18-1 229486-27-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

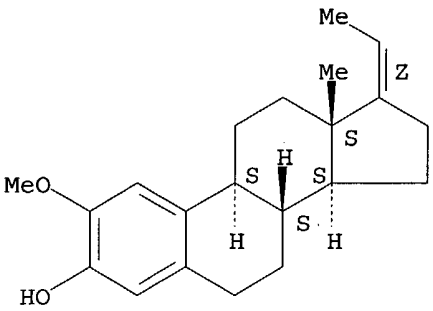
IT 858-98-0P 1667-98-7P 4736-62-3P 5774-17-4P 5779-47-5P 5976-73-8P
5976-74-9P 6599-97-9P 13879-55-5P 13879-57-7P 14030-45-6P
14846-63-0P 14982-15-1P 15001-40-8P 22787-09-3P 23880-59-3P
31559-52-1P 57711-40-7P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol
59452-15-2P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol
64215-82-3P 67519-62-4P 71716-18-2P 96111-26-1P 101766-63-6P
115208-23-6P 115387-92-3P 116627-15-7P 116627-20-4P 120574-27-8P
120574-28-9P 165619-18-1P 165619-19-2P 165619-20-5P 185910-40-1P
206442-55-9P 208758-44-5P 208758-45-6P 208758-46-7P 208758-49-0P
208758-50-3P 229486-06-0P 229486-07-1P 229486-08-2P 229486-09-3P

229486-10-6P 229486-11-7P 229486-12-8P 229486-13-9P 229486-14-0P
229486-15-1P 229486-16-2P **229486-17-3P** 229486-18-4P
229486-19-5P 229486-20-8P 229486-21-9P 229486-22-0P 229486-23-1P
229486-24-2P 229486-25-3P 229486-26-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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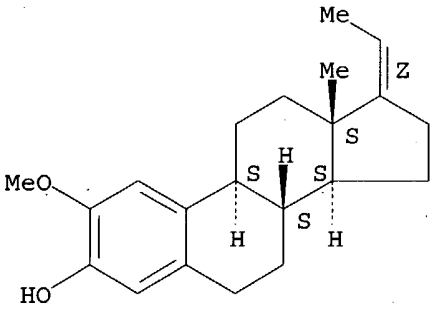
=> d bib abs hitstr tot

L21 ANSWER 1 OF 4 USPATFULL on STN
AN 2004:2032 USPATFULL
TI Systems and methods for rapid evaluation and design of molecules for predicted biological activity
IN Hendry, Lawrence B., Augusta, GA, UNITED STATES
PI US 2004002052 A1 20040101
AI US 2002-279546 A1 20021023 (10)
PRAI US 2001-344560P 20011023 (60)
US 2001-339954P 20011210 (60)
DT Utility
FS APPLICATION
LREP JOHN S. PRATT, ESQ, KILPATRICK STOCKTON, LLP, 1100 PEACHTREE STREET, SUITE 2800, ATLANTA, GA, 30309
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 2883
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The computer-based systems and methods are for rapidly evaluating molecules for suspected biological activity and relative potency, and for designing molecules for desired biological activity. The systems and

methods enable rapid screening of large molecular databases using one or more search engines designed to identify molecules predicted to possess specific biological activities.

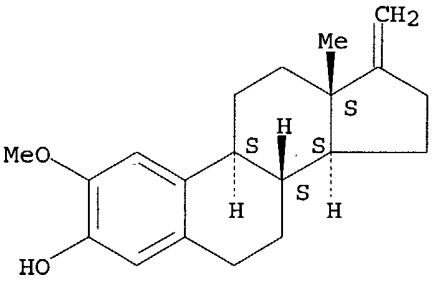
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **229486-17-3 431901-73-4**
(as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
RN 229486-17-3 USPATFULL
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 431901-73-4 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

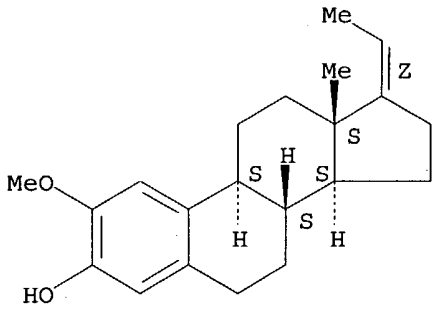


L21 ANSWER 2 OF 4 USPATFULL on STN
AN 2003:226354 USPATFULL
TI 2-substituted pregna-1,3,5(10) triene and chola-1,3,5(10) triene derivatives and their biological activity
IN Hesse, Robert Henry, Winchester, MA, UNITED STATES
Setty, Sundara Katugam Srinivasasetty, Cambridge, MA, UNITED STATES
Pechet, Maurice Murdoch, Cambridge, MA, UNITED STATES
Gile, Michael, Methuen, MA, UNITED STATES
PI US 2003158167 A1 20030821
AI US 2003-275257 A1 20030313 (10)
WO 2001-GB2103 20010511
DT Utility
FS APPLICATION
LREP BACON & THOMAS, PLLC, 625 SLATERS LANE, FOURTH FLOOR, ALEXANDRIA, VA, 22314
CLMN Number of Claims: 13

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 978
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I) in which: R.sup.1 represents a hydrogen atom or an O-protecting group; R.sup.2 represents a hydroxyl, lower alkoxy, carboxaldehyde, lower alk-1-enyl or hydroxy- or lower alkoxy-substituted lower alkyl group; R.sup.3 represents a methyl group having α- or β-configuration; X represents a C.sub.1-3 alkylene group or a valence bond; Y represents a carboxaldehyde group or a group of formula --C(R.sup.4)(R.sup.5)OR.sup.1 where R.sup.1 is as defined above and R.sup.4 and R.sup.5, which may be the same or different, are each selected from hydrogen atoms, alkyl, alkenyl and alkynyl groups such that the total carbon content of R.sup.4 and R.sup.5 does not exceed three atoms, with the proviso that X is a valence bond when both R.sup.4 and R.sup.5 are other than hydrogen; and the dotted line signifies that a double bond may optionally be present at the 16(17)-position exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **229486-17-3P**
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)
RN 229486-17-3 USPATFULL
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L21 ANSWER 3 OF 4 USPATFULL on STN
AN 2002:157823 USPATFULL
TI Antiangiogenic agents
IN Agoston, Gregory E., Germantown, MD, UNITED STATES
Shah, Jamshed H., Brookeville, MD, UNITED STATES
Hunsucker, Kimberly A., Germantown, MD, UNITED STATES
Pribluda, Victor S., Silver Spring, MD, UNITED STATES
LaVallee, Theresa M., Rockville, MD, UNITED STATES
Green, Shawn J., Vienna, VA, UNITED STATES
Herbstritt, Christopher J., Rockville, VA, UNITED STATES
Zhan, Xiaoguo H., Montgomery Village, MD, UNITED STATES
Treston, Anthony M., Rockville, MD, UNITED STATES
PI US 2002082433 A1 20020627
AI US 2001-939208 A1 20010824 (9)
RLI Continuation-in-part of Ser. No. US 2001-933894, filed on 21 Aug 2001, PENDING Continuation-in-part of Ser. No. US 2000-641327, filed on 18 Aug 2000, PENDING
PRAI US 2000-253385P 20001127 (60)

US 100023990PP1

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2	1449	1
3	IMIS	2
4	DISQ	1

Total number of pages: 10

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